ICU Management of Decompensated Cirrhosis

Endpoints of Resuscitation

- MAP ≥60-65 mmHg. In patients with acute renal failure or underlying hypertension, target MAP ≥ 65 mmHg.
- Urine output ≥0.5 ml/Kg/h.
- pH ≥7.20.
- Serum lactate levels can be inaccurate in patients with cirrhosis due to decreased lactate clearance.
- Request echocardiogram and consider PA catheter if multiple vasopressors are needed.

Fluid Resuscitation and Vasopressors

- Balanced crystalloid solutions, plasmalyte or LR, should be used over normal saline.
- Albumin is useful in patients with hepatorenal syndrome (HRS), spontaneous bacterial peritonitis (SBP), and post paracentesis circulatory dysfunction (PPCD). The recommended dose of albumin is:
    - 1 g/kg/d to a maximum of 100 g/d for HRS for two days and is continued for the duration of therapy along with vasopressors.
    - 1.5 g/Kg to a maximum of 100 g/d within 6 hours of diagnosis and 1 g/Kg on day 3 for SBP.
    - 6 to 8 g/L of ascites drained for large volume paracentesis.
- Norepinephrine is the vasopressor of choice.
- Vasopressin at 0.03 U/min (it can be increased up to 0.04 U/min) should be initiated if MAP ≥ 60-65 mmHg cannot be maintained with norepinephrine at 20-30 mcg/min.
- Epinephrine (it can be increased up to 30 mcg/min) should be initiated if MAP ≥60-65 mmHg cannot be maintained with norepinephrine at 30 mcg/min and vasopressin at 0.04 U/min.
- If MAP ≥65 mmHg cannot be maintained with norepinephrine at 30 mcg/min, vasopressin at 0.04 U/min, and epinephrine at 30 mcg/min, increase norepinephrine up to 90 mcg/min. Higher doses of vasopressors are unlikely to be beneficial after reaching these parameters.
- Patients with cirrhosis usually have a hyperdynamic status with high cardiac output. However, a subset of patients can present or develop a hypodynamic status with reduced LV function. In this subset, in addition to investigating and treating the etiology, an inodilator, dobutamine or milrinone can be added to the vasopressors.
- In patients with atrial fibrillation with rapid ventricular response, consider use of phenylephrine instead of norepinephrine or epinephrine.

Ascites

- Diagnostic and therapeutic paracentesis is the first-line treatment for large ascites.
    - Diagnostic paracentesis to rule out SBP should be considered regardless of therapeutic indication.
    - Therapeutic paracentesis if associated with abdominal hypertension.
        - Avoid large volume paracentesis (removing >5 L) to prevent decrease in effective intravascular volume which results from:

    - Vasodilatation “post-paracentesis circulatory dysfunction”
    - Volume loss
- Albumin IV infusion at a dose of 6–8 g/L ascites drained if large volume paracentesis.
    - Consider albumin IV infusion regardless of amount of ascites removed.
    - If used, drains should be removed within 48 hours.
- TIPS is usually reserved for patients with refractory ascites.

Hepatorenal Syndrome (HRS)

Definition

HRS occurs due to functional reduction in circulatory volume to kidneys which is unresponsive to volume expansion. Diagnosis of HRS requires exclusion of other causes of kidney injury.

Diagnostic Criteria:

- Presence of cirrhosis, acute liver failure, or acute-on-chronic liver failure.
- Increase in serum creatinine ≥ 0.3 mg/dl within 48 hours or ≥ 50% from baseline value and or urine ≤ 0.5 ml/kg for ≥ 6 hours.
- No response after at least two days of diuretic withdrawal and volume expansion with balanced crystalloids and albumin.
    - The recommended dose of albumin is 1 g/kg/d to a maximum of 100 g/d.
- Absence of shock.
- Absence of parenchymal disease as indicated by proteinuria >500 mg/day, microhematuria (>50 red blood cells per high power field), and or abnormal renal ultrasonography.
- Suggestion of renal vasoconstriction with fractional excretion of sodium (FENa) of < 0.2%. FENa has historically been considered unhelpful in distinguishing HRS from ATN. However, it appears that FENa, with a new lower cut-off of 0.2% may in fact be clinically useful for distinguishing HRS from ATN.

Classification:
The old terms HRS type 1 and type 2 have been replaced with HRS-AKI and HRS-NAKI.
HRS-AKI is defined as:

- Absolute increase in sCr ≥0.3 mg/ dL within 48 hours or ≥50%, and/or
- Urine output ≤ 0.5 ml/kg for ≥ 6 hours, or
- Percent increase in sCr ≥ 50% using the last available value of outpatient SCr within 3 months as the baseline value

Functional kidney injury in cirrhotic patients who do not meet the criteria of HRS-AKI is termed HRS-NAKI (HRS-Non-AKI) and is based on estimated glomerular filtration rate (eGFR) rather than the serum creatinine.

HRS-NAKI is further divided into two subtypes:

- HRS - Acute Kidney Disease (HRS-AKD) is defined as:
    - Percent increase in sCr < 50%, using the last available value of outpatient, within three months as the baseline value.
- HRS - chronic kidney disease (HRS-CKD) is defined as:
    - eGFR < 60 ml/min per 1.73 m2 for ≥ 3 months in absence of other (structural) causes

HRS Treatment

Norepinephrine IV infusion in combination with albumin with the goal of raising the MAP by 10 mmHg to treat for a total of two weeks**.**

- Albumin 25% 1 g/kg/d to a maximum of 100 g/d for HRS for two days and is continued at 20 to 50 g/day for the duration of therapy along with norepinephrine.
- Norepinephrine IV infusion started at a dose of 0.5mg/h to achieve an increase in MAP of at least 10 mmHg. It can be increased by 0.5 mg/h to a maximum dose of 3 mg/h in case the parameter is not met.
- Terlipressin, a vasopressin analogue, is the most common vasoconstrictor used worldwide, and both U.S. and European guidelines recommend it as a first-line agent for HRS-AKI (see fig 1). In 2023 was approved in the USA but remains very expensive.
    - Improves renal function and maybe mortality.
    - Administer 1 mg IV q6h as IV bolus and measure sCr on day 4:
        - if sCr decreases by <30% % from baseline, increase dose of terlipressin to 2 mg IV q6h.
        - Continue treatment until two consecutive measurements ≥2 hr apart of sCr of ≤1.5 mg/dl to a maximum duration 14 days.
    - Compared with vasopressin has a longer half-life and a more predictable therapeutic window which allows for bolus administration through a peripheral IV.
        - Does not require ICU monitoring and can be administered IV through a peripheral line.
    - It is associated with an increased incidence of respiratory failure due to pulmonary edema.
        - It is essential to withhold terlipressin and albumin if there is clinical evidence of intravascular volume overload or elevated RVSP on echocardiogram.
        - It should not be given if O2Sat <90%.

GI bleeding

- Ceftriaxone x7 days regardless of whether it is variceal or non-variceal.
- PPI IV for peptic ulcer disease and for stress prophylaxis.
- Octreotide IV for esophageal and or gastric varices.
- Endoscopy within 12 hours.
- PRBC transfusion to maintain hemoglobin > 7g/dl.
- Platelet transfusion to correct the platelet count to >50 000.
- The use of FFP has not been properly evaluated in patients with GI bleeding and cirrhosis. It is important to note that PT/INR is a marker of liver function and not of coagulation disorder in patients with cirrhosis.
- Vitamin K 10 mg IV weekly (should be given regardless GI bleeding).
- TIPS for recurrent or persistent variceal bleed.

VTE prophylaxis should follow standard of care

- The timing of VTE prophylaxis initiation should not differ from patients without decompensated cirrhosis, regardless of standard coagulation test results.

    - Enoxaparin is the VTE prophylactic agent of choice outside of renal failure. Bleeding complications may be more common with unfractionated as compared with low molecular weight heparin.
- In patients with cirrhosis, reductions in liver-derived procoagulants are offset by reductions in anticoagulants as well. Patients with decompensated cirrhosis are at risk for bleeding as well as thrombosis.
- Importantly, the most common VTE event in decompensated cirrhosis is portal vein thrombosis, which can lead to reduced hepatic perfusion, increased variceal pressure, worsening hepatic decompensation, and technical issues with future transplantation.

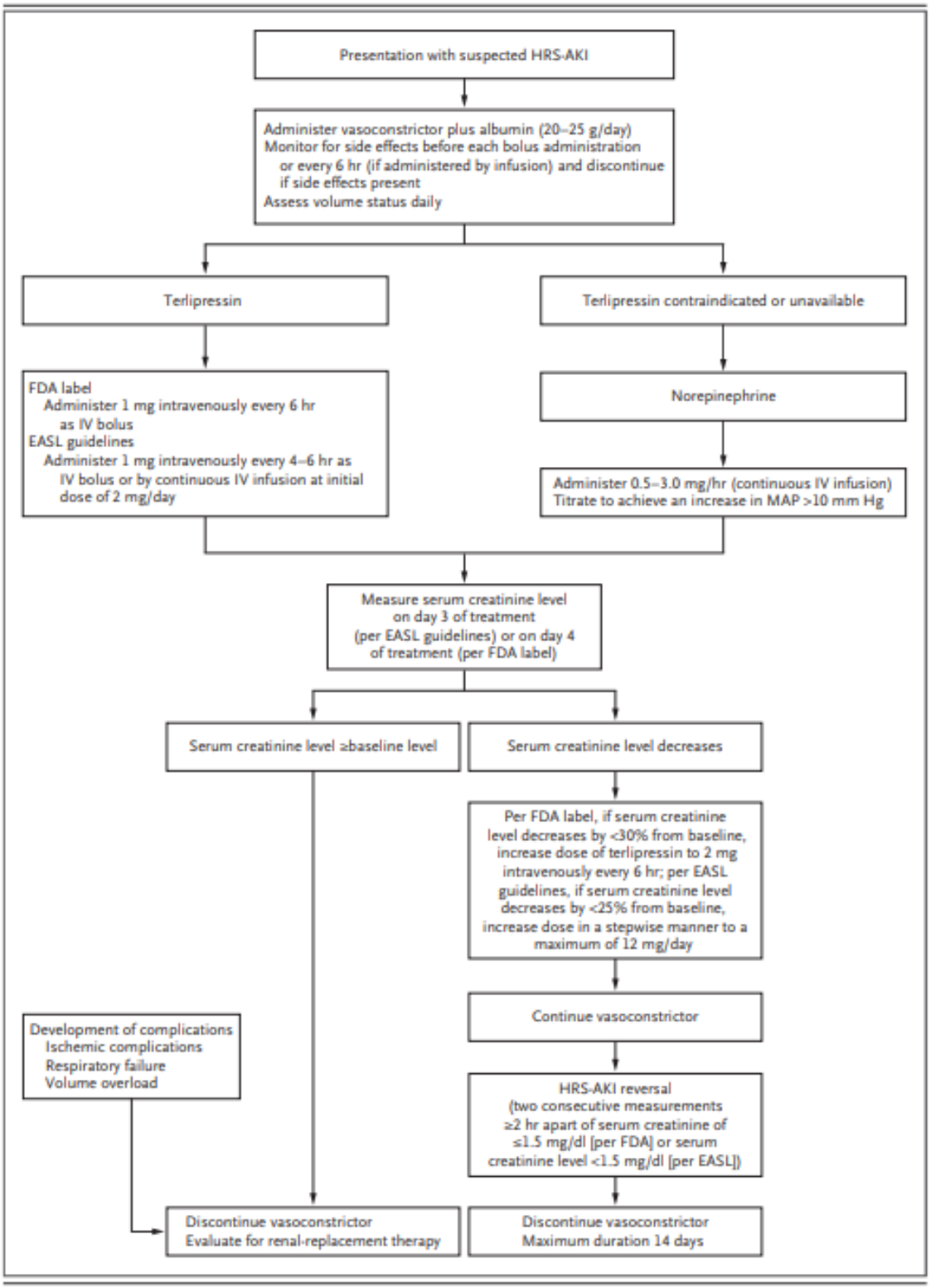
Hepatic encephalopathy

- Ammonia levels should be obtained to exclude or implicate hepatic encephalopathy as an etiology of altered mental status, but not to follow its progression or response to therapy.
- Initial treatment should include lactulose. The dose should be titrated to achieve two to three bowel movements per day.
- For patients who have not improved within 48 hours, rifaximin should be added at 550 mg every 12 hours. For patients who cannot take lactulose, rifaximin should be initiated.
- Correction of hypokalemia is essential since hypokalemia increases renal ammonia production.

Early enteral nutrition

Early enteral nutrition should be provided to patients with decompensated cirrhosis unless there are clear contraindications.

Fig 1. HRS-AKI management



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